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     FILE 'HCAPLUS' ENTERED AT 11:25:28 ON 26 FEB 2002
                E OSTEOSCREEN/PA,CS
L1           13 S E3-E12
                E OESTEOSCREEN/PA,CS
                E MUNDY G/AU
L2          256 S E3,E6,E8-E10
                E GARRETT  R/AU
                E GARRETT R/AU
L3           55 S E3
                E GARRETT ROSS/AU
L4            7 S E3,E4
                E ROSSINI G/AU
L5           80 S E3-E16
                E GARRETT I/AU
L6           53 S E3-E7
L7          422 S L1-L6
L8            4 S L7 AND ?PROTEASOM?

     FILE 'REGISTRY' ENTERED AT 11:29:20 ON 26 FEB 2002
L9            1 S 140879-24-9

     FILE 'HCAPLUS' ENTERED AT 11:30:15 ON 26 FEB 2002
L10        2944 S L9
L11        4723 S PROTEASOME OR PROSOME OR (26S OR 26 S)(L)PROTEASE OR IMMUNOPR
L12          21 S  TRICORN ()(PROTEASE OR PROTEINASE)
L13           4 S L7 AND L10-L12
L14           4 S L8,L13
L15       11143 S NF (L) KAPPA (L) B
L16        8204 S NUCLEAR (L) FACTOR (L) KAPPA (L) B
L17           4 S L7 AND L15,L16
L18           5 S L14,L17
L19          21 S EPOXOMICIN# OR EPOXOMYCIN#
L20          41 S PS341 OR PS 341
L21          46 S NLVS
                E ALDEHYDE/CT
L22         166 S E15(L)(PEPTIDE OR PEPTIDYL)
L23        1055 S E15+NT(L)(PEPTIDE OR PEPTIDYL)

     FILE 'REGISTRY' ENTERED AT 11:40:11 ON 26 FEB 2002
L24           1 S 6493-05-6
L25           1 S 133343-34-7
L26           7 S LACTACYSTIN
L27           3 S L26 AND C15H24N2O7S
L28          19 S C15H24N2O7S/MF
L29           6 S L28 AND NC4/ES AND 1/NR
L30           3 S L29 NOT (T/ELS OR GLYCINE)
L31           1 S 134381-21-8
L32           9 S C28H50N4O7/MF
L33           3 S L32 AND OC2/ES AND 1/NR
L34           2 S L33 NOT T/ELS
L35           1 S 179324-69-7
L36           1 S C19H25BN4O4/MF AND NC2NC2/ES AND 46.150.18/RID AND 2/NR
L37           1 S 158442-41-2
L38          41 S C32H50N4O8/MF
L39          14 S L38 AND 4/SQL
L40           3 S L39 AND 46.150.18/RID AND 1/NR
L41           1 S 193482-49-4
L42           3 S C28H43IN4O8S/MF
L43           2 S L42 NOT 125I
L44          10 S L24,L25,L30,L31,L34,L35,L36,L37,L41,L43
                SEL RN
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L45          16 S E1-E10/CRN
L46           3 S L45 NOT MXS/CI
L47          13 S L44,L46
L48          13 S L45 NOT L47

     FILE 'HCAPLUS' ENTERED AT 11:49:48 ON 26 FEB 2002
L49        1978 S L47
L50           5 S L48
L51         548 S LACTACYSTIN#
L52        2396 S PTX
L53        4729 S L19-L22,L49-L52

     FILE 'REGISTRY' ENTERED AT 11:50:44 ON 26 FEB 2002
L54             STR
L55           3 S L54
L56             STR L54
L57           1 S L56
                SAV L44 GITOMER1/A TEMP
                SAV L45 GITOMER2/A TEMP
                DEL GITOMER1/A
                DEL GITOMER2/A
                SAV TEMP L47 GITOMER1/A
                SAV TEMP L48 GITOMER2/A
                SAV L56 GITOMER3/Q

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L58           3 S L7 AND L53
L59           5 S L18,L58

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FILE COVERS 1907 - 26 Feb 2002  VOL 136 ISS 9
FILE LAST UPDATED: 25 Feb 2002  (20020225/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the
CAS Registry Numbers that were added to the CAS files between 12/27/01
and 1/23/02.  As of 1/23/02, the situation has been resolved.  Searches
and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry
Numbers with the P indicator executed between 12/27/01 and 1/23/02 may
be incomplete.  See the NEWS message on this topic for more information.

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L59 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:300537 HCAPLUS
DN 134:331618
TI Inhibitors of **proteasomal** activity for stimulating bone and hair growth
IN **Mundy, Gregory R.; Garrett, Ross I.; Rossini, G.**
PA **Osteoscreen, Inc., USA**
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-06
ICS A61K038-07; A61K038-13; A61K031-165; A61K031-365; A61K031-4015; A61K031-522; A61P019-00; A61P043-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 62
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001028579	A2	20010426	WO 2000-US41360	20001020
WO 2001028579	A3	20010920		

W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

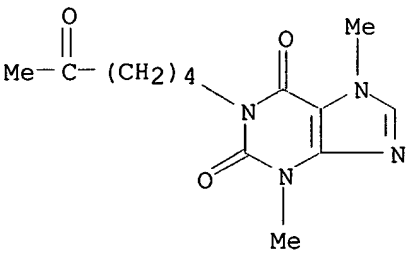
PRAI US 1999-421545 A 19991020
US 2000-558973 A 20000425

AB Compds. that inhibit the activity of **NF-.kappa.B** or inhibit the activity of the **proteasome** or both promote bone formation and hair growth and are thus useful in treating osteoporosis, bone fracture or deficiency, primary or secondary hyperparathyroidism, periodontal disease or defect, metastatic bone disease, osteolytic bone disease, post-plastic surgery, post-prosthetic joint surgery, and post-dental implantation; they also stimulate the prodn. of hair follicles and are thus useful in stimulating hair growth, including hair d., in subject where this is desirable. N-carbobenzyol-Ile-Glu-(OtBu)Ala-Leu-CHO (PSI) in 50% propylene glycol, 10% DMSO, and 40% water was injected daily for 5 days (1mg/kg body wt./day) into the s.c. tissue of mice and the tissue was examd. histol. 16 days later. The no. of hair follicles increased and the downward extension of these hair follicles into the dermal tissue was noted, which are hallmarks of anagen. There was an obvious increase in size of the follicle diam. and the root sheath diam.

ST **proteasome** inhibitor hair bone growth stimulant
IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(I.**kappa.B** (inhibitor of **NF-.kappa.B**); inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Periodontium
Tooth
(disease; inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Hair
(follicle; inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Bone, disease
(fracture; inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Bone
Hair preparations
(growth stimulants; inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Dental materials and appliances
(implants; inhibitors of **proteasomal** activity for stimulating

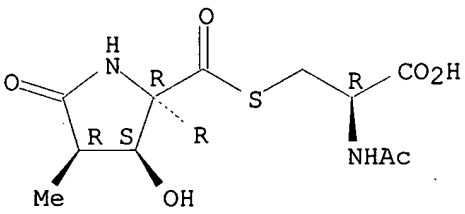
bone and hair growth)
IT Bone formation
(inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Bone morphogenetic proteins
Estrogens
Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Bone, disease
(metastatic and osteolytic; inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteogenins; inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Surgery
(post-plastic; inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Hyperparathyroidism
(secondary; inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Phosphoproteins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(statins; inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Joint, anatomical
(surgery of; inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Osteoporosis
(therapeutic agents; inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT 13598-36-2D, Phosphonic acid, alkylidenebis- derivs.
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bisphosphonate; inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT 67-99-2, Gliotoxin 404-86-4, Capsaicin **6493-05-6, PTX** 9035-81-8, Trypsin inhibitor 25769-03-3, PDTC 59865-13-3, Cyclosporin a 65240-86-0, PPM 18 79902-63-9, Simvastatin 110044-82-1 110115-07-6 **133343-34-7, Lactacystin** 133407-82-6, MG 132 133407-86-0, MG 115 **134381-21-8, Epoxomicin** **158442-41-2D**, PSI, epoxides 179324-22-2, MG 262 **179324-69-7, PS 341** 336099-20-8 336099-21-9 336608-38-9, Bay 11-7082
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT **140879-24-9, Proteasome**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT **6493-05-6, PTX 133343-34-7, Lactacystin 134381-21-8, Epoxomicin** **158442-41-2D**, PSI, epoxides **179324-69-7, PS 341**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of **proteasomal** activity for stimulating bone and hair growth)
RN 6493-05-6 HCAPLUS

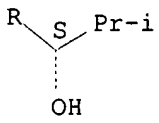
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



RN 133343-34-7 HCAPLUS
CN L-Cysteine, N-acetyl-, (2R,3S,4R)-3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-4-methyl-5-oxo-2-pyrrolidinecarboxylate (ester) (9CI) (CA INDEX NAME)

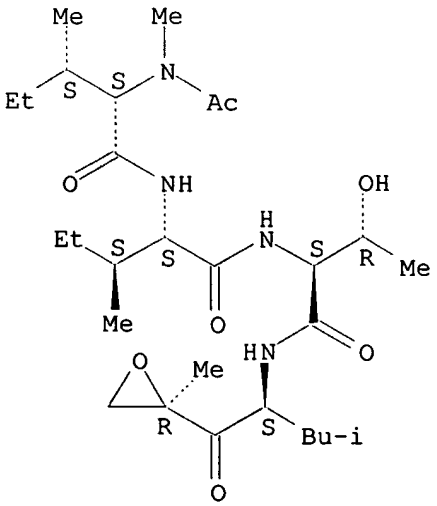
Absolute stereochemistry. Rotation (+).





RN 134381-21-8 HCAPLUS
CN L-Threoninamide, N-acetyl-N-methyl-L-isoleucyl-L-isoleucyl-N-[(1S)-3-methyl-1-[[(2R)-2-methyloxiranyl]carbonyl]butyl]- (9CI) (CA INDEX NAME)

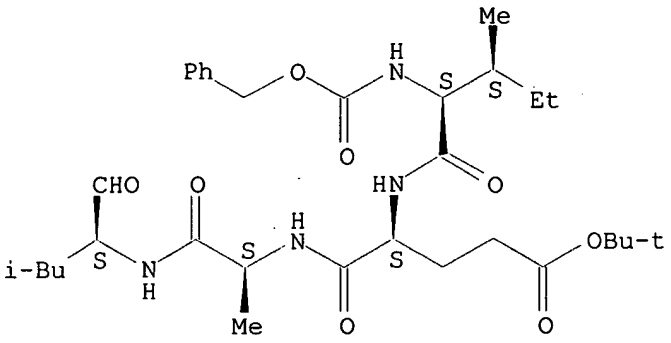
Absolute stereochemistry.



RN 158442-41-2 HCAPLUS
CN L-Alaninamide, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-L-.alpha.-glutamyl-

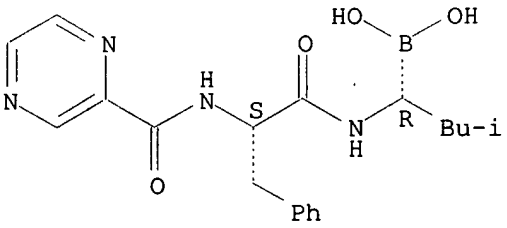
N-[(1S)-1-formyl-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 179324-69-7 HCAPLUS
CN Boronic acid, [(1R)-3-methyl-1-[[(2S)-1-oxo-3-phenyl-2-[(pyrazinylcarbonyl)amino]propyl]amino]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **140879-24-9, Proteasome**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; inhibitors of **proteasomal** activity for stimulating bone and hair growth)
RN 140879-24-9 HCAPLUS
CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L59 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:240712 HCAPLUS
DN 135:18367
TI Therapeutic efficacy of a soluble receptor activator of **nuclear factor .kappa.B**-IgG Fc fusion protein in suppressing bone resorption and hypercalcemia in a model of humoral hypercalcemia of malignancy
AU Oyajobi, Babatunde O.; Anderson, Dirk M.; Traianedes, Kathy; Williams, Paul J.; Yoneda, Toshiyuki; **Mundy, Gregory R.**
CS Division of Endocrinology, Department of Medicine, University of Texas Health Science Center at San Antonio, San Antonio, TX, 78229, USA
SO Cancer Res. (2001), 61(6), 2572-2578
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
CC 15-5 (Immunochemistry)
AB Receptor activator of **NF-.kappa.B** (RANK) is a membrane-bound tumor necrosis factor receptor homolog that mediates signals obligatory for osteoclastogenesis as well as osteoclast activation and survival in vivo. The present study was undertaken to evaluate the efficacy of a sol. murine RANK-human Ig fusion protein (muRANK.Fc) as a

bone resorption inhibitor in vitro and in vivo. The in vitro studies demonstrated the ability of muRANK.Fc to inhibit human parathyroid hormone-related protein (PTHrP)-induced resorption in fetal rat long bone cultures. Short-term administration of muRANK.Fc to normal growing mice resulted in a complete disappearance of osteoclasts from metaphyses of long bones assocd. with a pronounced increase in calcified trabeculae and bone radiodensity. In a model of humoral hypercalcemia of malignancy in which PTHrP secreted by s.c. xenografts of human lung cancer in nude mice induces extensive osteolysis and severe hypercalcemia, daily administration of muRANK.Fc from time of tumor implantation profoundly inhibited osteoclastic bone resorption and prevented hypercalcemia. MuRANK.Fc had no effect on tumor prodn. of PTHrP, because there was no difference between circulating human PTHrP levels in muRANK.Fc-treated and vehicle-treated tumor-bearing mice. Moreover, even when treatment was initiated after hypercalcemia was established, muRANK.Fc attenuated further increases in blood ionized calcium. These data demonstrate the potent anti-resorptive effects of muRANK.Fc in vivo as well as highlight the potential utility of disrupting RANK signaling as a novel therapeutic approach in humoral hypercalcemia of malignancy and possibly multiple myeloma and skeletal metastases assocd. with osteolysis.

ST RANK IgG Fc fusion protein bone resorption hypercalcemia malignancy

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G, Fc, fusion protein contg.; therapeutic efficacy of sol. receptor activator of **NF-.kappa.B**-IgG Fc fusion protein in suppressing bone resorption and hypercalcemia in humoral hypercalcemia of malignancy model)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RANK, sol., fusion protein contg.; therapeutic efficacy of sol. receptor activator of **NF-.kappa.B**-IgG Fc fusion protein in suppressing bone resorption and hypercalcemia in humoral hypercalcemia of malignancy model)

IT Neoplasm
(humoral hypercalcemia of malignancy; therapeutic efficacy of sol. receptor activator of **NF-.kappa.B**-IgG Fc fusion protein in suppressing bone resorption and hypercalcemia in humoral hypercalcemia of malignancy model)

IT Osteoclast
(inhibition; therapeutic efficacy of sol. receptor activator of **NF-.kappa.B**-IgG Fc fusion protein in suppressing bone resorption and hypercalcemia in humoral hypercalcemia of malignancy model)

IT Bone
(resorption, inhibitors; therapeutic efficacy of sol. receptor activator of **NF-.kappa.B**-IgG Fc fusion protein in suppressing bone resorption and hypercalcemia in humoral hypercalcemia of malignancy model)

IT Signal transduction, biological
(therapeutic efficacy of sol. receptor activator of **NF-.kappa.B**-IgG Fc fusion protein in suppressing bone resorption and hypercalcemia in humoral hypercalcemia of malignancy model)

IT 7440-70-2, Calcium, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(hypercalcemia; therapeutic efficacy of sol. receptor activator of **NF-.kappa.B**-IgG Fc fusion protein in suppressing bone resorption and hypercalcemia in humoral hypercalcemia of malignancy model)

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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L59 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:741943 HCAPLUS
DN 133:291099
TI Treatment of myeloma bone disease with **proteasomal** and **NF-.kappa.B** activity inhibitors
IN **Mundy, Gregory R.**
PA **Osteoscreen, Inc., USA**
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-04
ICS A61K031-40; A61K031-166; A61P019-08
CC 1-6 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000061167	A2	20001019	WO 2000-US9121	20000407
	WO 2000061167	A3	20010111		
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1169049	A2	20020109	EP 2000-921764	20000407
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1999-289229	A	19990409		
	WO 2000-US9121	W	20000407		

AB The present invention involves the identification and use of compns. for treating myeloma bone disease. The compns. inhibit **proteasomal** activity and decrease the activity of the transcription factor **NF**

-.**kappa.B**. Assessment of a candidate compd. for its ability to inhibit prodn. or activity of **proteasomal** enzymes or **NF-.kappa.B** provides a useful means to identify agents to treat myeloma bone disease.

ST bone myeloma therapy **proteasome** NFkappaB inhibitor; **proteasome** inhibitor bone myeloma therapy; NF kappaB inhibitor bone myeloma therapy

IT Transcription **factors**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**NF-.kappa.B** (**nuclear factor .kappa.B**); treatment of myeloma bone disease with **proteasomal** and **NF-.kappa.B** activity inhibitors)

IT Antitumor agents
(multiple myeloma; treatment of myeloma bone disease with **proteasomal** and **NF-.kappa.B** activity inhibitors)

IT 5108-96-3 65240-86-0, Ppm-18 **158442-41-2**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of myeloma bone disease with **proteasomal** and **NF-.kappa.B** activity inhibitors)

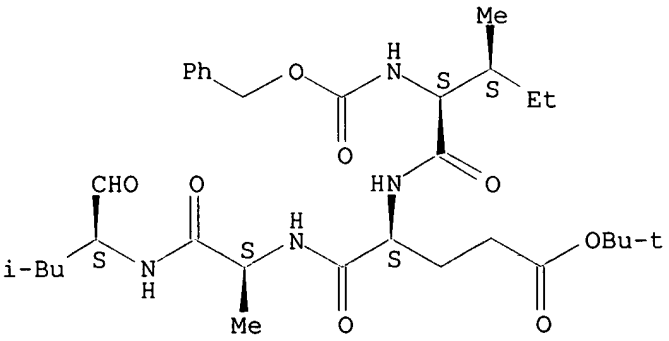
IT **140879-24-9, Proteasome**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(treatment of myeloma bone disease with **proteasomal** and **NF-.kappa.B** activity inhibitors)

IT **158442-41-2**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of myeloma bone disease with **proteasomal** and **NF-.kappa.B** activity inhibitors)

RN 158442-41-2 HCAPLUS

CN L-Alaninamide, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-L-.alpha.-glutamyl-N-[(1S)-1-formyl-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **140879-24-9, Proteasome**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(treatment of myeloma bone disease with **proteasomal** and **NF-.kappa.B** activity inhibitors)

RN 140879-24-9 HCAPLUS

CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L59 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:478627 HCAPLUS

DN 133:247623

TI Patterns of gene expression associated with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A

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SO J. Bone Miner. Metab. (2000), 18(3), 132-139
CODEN: JBMME4; ISSN: 0914-8779
PB Springer-Verlag Tokyo
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
AB The pluripotent mesenchymal stem cells give rise to osteoblasts, adipocytes, chondrocytes, and myoblasts. The differentiation of these stem cells into each of the mature functional cells may be controlled by a distinctive master gene(s) and is assocd. with temporal and spatial expression of diverse genes. Identification of genes that are expressed during the differentiation of the mesenchymal cells to osteoblasts is, therefore, important to obtain insights into the mol. mechanisms of osteogenesis. The murine undifferentiated mesenchymal cell 3T3-F442A, when treated with the bone morphogenetic protein 2 (BMP-2), a well-characterized inducer of mesenchymal cell differentiation, exhibited both osteoblastic and adipocytic differentiation. Using the SAGE (serial anal. of gene expression) technique, which has been shown to enable quant. anal. of large nos. of genes in a simple and quick manner, the authors obtained 1600 sequence tags representing 2107 individual nucleotide sequences from control and BMP-2-treated 3T3-F442A cells, resp. By comparing the frequency of tag occurrence, the authors found profiles of up- or downregulated genes assocd. with osteoblast or adipocyte phenotype such as type I collagen, osteonectin and OSF-2, or C/EBP.beta., aP2, fatty acid synthase, and lipoprotein lipase, resp., in BMP-2-treated 3T3-F442A cells. The authors' data show that BMP-2 induces not only osteoblastic but also adipocytic differentiation in the 3T3-F442A cells. They also show that the 3T3-F442A cells have bipotentials of differentiating toward osteoblasts and adipocytes. The results, therefore, might explain the inverse correlation between trabecular bone vol. and fat vol. in the bone marrow cavity. The results also suggest that the SAGE may be a useful technique that allows a fast and efficient way to generate global and local views of gene expression assocd. with cellular differentiation of the mesenchymal stem cells.
ST BMP2 gene expression osteoblast adipocyte differentiation
IT Bone morphogenetic proteins
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(2; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Antigens
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(AD1; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Chaperonins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(ADP ribosylation factor-like protein 2; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Transcription factors
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(AP-2 (activator protein 2); patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT RNA formation factors
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(C/EBP-.beta. (CCAAT box/enhancer element-binding protein .beta.);

patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Transcription factors
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(Cis2; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT G proteins (guanine nucleotide-binding proteins)
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(Gs (adenylate cyclase-stimulating), .alpha.-subunit; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Histones
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(H2A; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Heat-shock proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(HSC73; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(J1; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(L12; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(L22; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(L32; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(L37a; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(L5; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(OSF-2 (osteoblast-specific factor-2); patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(S16; patterns of gene expression assocd. with BMP-2-induced osteoblast

and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(S2, S28; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(S24; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(S29; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(TNF-induced protein complex .gamma.; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Phosphoproteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(acidic ribosomal protein P2; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Phosphoproteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(acidic ribosomal, P1; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Phosphoproteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(acidic ribosomal, P0; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Phosphoproteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(adducins, human erythrocyte, .alpha.-subunit; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Adipose tissue
(adipocyte, differentiation; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Cell differentiation
(adipocyte; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(calcylin; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(calgizzarins; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell

3T3-F442A)
IT Chaperonins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(chaperone CCTB; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Osteoblast
(differentiation; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(human ribosomal protein S20; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(human ribosomal protein S7; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(hydrophobic protein MTF; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(insulin-stimulated eIF-4E binding protein; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(jesolin; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Transcription factors
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(junB; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(minopontins; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(mitochondrial ATPase inhibitor; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Cell differentiation
(osteoblast; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT Transcription factors
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)

(p68-c-rel; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Bone formation
(patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Gene, animal
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Chloride channel
Fibroblast growth factor receptors
Macrophage migration inhibitory factor
Osteonectin
Ribosomal proteins
Tau factor
Tubulins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(protein for hereditary multiple exostosis; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(rat brain protein; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(rat ribosomal protein L23A; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(rat ribosomal protein S19; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(rpA2; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Embryo, animal
(stem cell; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Collagens, biological studies
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(type I; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Anion channel
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(voltage-dependent 3; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal

progenitor cell 3T3-F442A)
IT G proteins (guanine nucleotide-binding proteins)
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(.beta.-subunit; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT **140879-24-9, Proteasome**
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(Rc7-I; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT 147014-97-9, CDK4 kinase
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(inhibitor; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT 9004-02-8, Lipoprotein lipase 9007-43-6, Cytochrome c, biological studies 9036-37-7, Aminolevulinic acid dehydrogenase 9045-77-6, Fatty acid synthase 9059-25-0, Lysyl oxidase 9059-32-9, GTPase 60616-82-2, Cathepsin L
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT 9001-16-5, Cytochrome c oxidase
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(subunit VIII; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
IT 37205-63-3, ATP synthase
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(.gamma.-chain precursor and hydrogen-transporting; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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IT **140879-24-9, Proteasome**
RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(Rc7-I; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
RN 140879-24-9 HCAPLUS
CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L59 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:53374 HCAPLUS
DN 132:102860
TI Inhibitors of **proteasomal** activity for stimulating bone and hair growth
IN **Mundy, Gregory R.; Garrett, I. Ross; Rossini, G.**
PA **Osteoscreen, USA**
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 1-12 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000002548	A2	20000120	WO 1999-US15533	19990709
W: AL, AM, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SD, SG, SI, SK, TR, TT, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9963109	A1	20000201	AU 1999-63109	19990709
EP 1096924	A1	20010509	EP 1999-933827	19990709
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI US 1998-113947	A1	19980710		
WO 1999-US15533	W	19990709		

AB Compds. that inhibit the activity of **NF-.kappa.B** or inhibit the activity of the **proteasome** or both promote bone formation and hair growth and are thus useful in treating osteoporosis, bone fracture or deficiency, primary or secondary hyperparathyroidism, periodontal disease or defect, metastatic bone disease, osteolytic bone disease, post-plastic surgery, post-prosthetic joint surgery, and post-dental implantation. They also stimulate the prodn. of hair follicles and are thus useful in stimulating hair growth, including hair d., in subject where this is desirable.
ST hair bone growth stimulation NFkappaB inhibitor; **proteasome** inhibitor hair bone growth stimulation
IT Transcription **factors**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-.kappa.B (nuclear factor .kappa.B); NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT Bone formation
Drug delivery systems
Drug screening
(**NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Bone morphogenetic proteins
Estrogens
Growth factors, animal
Hormones, animal, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth, and use with other agents)
IT Antitumor agents
(bone, metastasis; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Skull
(calvarium, calvarial bone growth assay; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Cartilage
(cartilage-derived morphogenetic proteins; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth, and use with other agents)
IT Joint, anatomical
(degeneration; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Disease, animal
(dental; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Periodontium
(disease; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Hair
(follicle; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Bone, disease
(fracture, and bone deficiency; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Bone
(growth promoters; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth, and use with other agents)
IT Hair preparations
(growth stimulants; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Dental materials and appliances
(implants, post-dental implantation; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Cell differentiation
(inducers; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth, and use with other agents)
IT Bone, neoplasm
(metastasis, inhibitors; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(morphogenetic, cartilage-derived; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth, and use with other agents)
IT Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteogenins; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth, and use with other agents)
IT Bone, disease
(osteolytic; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Isoprenoids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pathway; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptidic aldehydes; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT **Aldehydes, biological studies**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**peptidyl; NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Surgery
(plastic, post-plastic surgery; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Joint, anatomical
Prosthetic materials and Prosthetics
(post-prosthetic joint surgery; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Hyperparathyroidism
(primary; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**proteasome; NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Bone
(resorption, inhibitors; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth, and use with other agents)
IT Hyperparathyroidism
(secondary; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Osteoporosis
(therapeutic agents; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
IT Drug delivery systems
(topical; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and

hair growth)

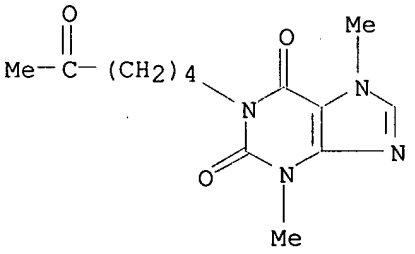
IT 67-99-2, Gliotoxin 404-86-4, Capsaicin **6493-05-6**, Pentoxifylline 59865-13-3, Cyclosporin A 79902-63-9, Simvastatin 106096-93-9, Basic fibroblast growth factor 110044-82-1 110115-07-6 **133343-34-7**, **Lactacystin** 133407-82-6, MG 132 133407-86-0, MG 115 **158442-41-2** 179324-22-2, MG 262
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT **140879-24-9**, **Proteasome**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)

IT 13598-36-2D, Phosphonic acid, bisphosphonates
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and statins; **NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth, and use with other agents)

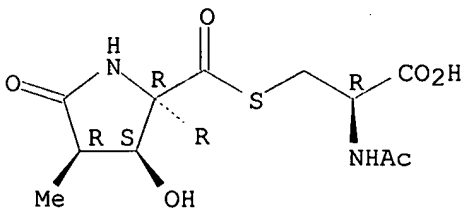
IT **6493-05-6**, Pentoxifylline **133343-34-7**, **Lactacystin** **158442-41-2**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)

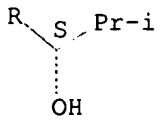
RN 6493-05-6 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



RN 133343-34-7 HCAPLUS
CN L-Cysteine, N-acetyl-, (2R,3S,4R)-3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-4-methyl-5-oxo-2-pyrrolidinecarboxylate (ester) (9CI) (CA INDEX NAME)

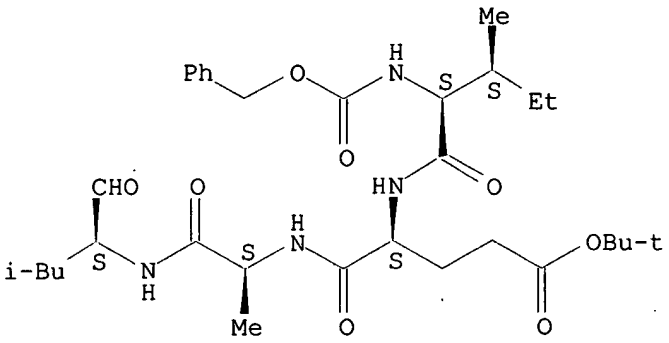
Absolute stereochemistry. Rotation (+).





RN 158442-41-2 HCAPLUS
CN L-Alaninamide, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-L-.alpha.-glutamyl-N-[(1S)-1-formyl-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **140879-24-9, Proteasome**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**NF-.kappa.B** inhibitors and inhibitors of **proteasomal** activity for stimulating bone and hair growth)
RN 140879-24-9 HCAPLUS
CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

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L193 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:745665 HCAPLUS
DN 130:94381
TI **NF-.kappa.B** activation provides the potential link between inflammation and hyperplasia in the **arthritic joint**
AU Miagkov, Alexei V.; Kovalenko, Dmitry V.; Brown, Chadwick E.; Didsbury, John R.; Cogswell, John P.; Stimpson, Stephen A.; Baldwin, Albert S.; Makarov, Sergei S.
CS Thurston Arthritis Research Center, University of North Carolina, Chapel Hill, NC, 27599, USA
SO Proc. Natl. Acad. Sci. U. S. A. (**1998**), 95(23), 13859-13864
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
CC 15-8 (Immunochemistry)
Section cross-reference(s): 3
AB The transcription factor **NF-.kappa.B** is a pivotal regulator of inflammatory responses. While the activation of **NF-.kappa.B** in the **arthritic**

in animal models of rheumatoid arthritis)
IT Inflammation
(synovitis; **NF-.kappa.B** activation in inflamed synovium activates inflammatory cytokines but inhibits TNF.alpha.- and FasL-mediated apoptosis thereby promoting hyperplasia in animal models of rheumatoid arthritis)
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(2) Baldwin, A; Annu Rev Immunol 1996, V14, P649 HCAPLUS
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(31) Zvaifler, N; Am J Pathol 1997, V150, P1125 MEDLINE

L193 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:263658 HCAPLUS
DN 129:15209
TI Activation of **NF-.kappa.B** is involved in the survival of **osteoclasts** promoted by interleukin-1
AU Jimi, Eijiro; Nakamura, Ichiro; Ikebe, Tetsuro; Akiyama, Shuichi; Takahashi, Naoyuki; Suda, Tatsuo
CS Dep. Biochem., School Dentistry, Showa Univ., Tokyo, 142-8555, Japan
SO J. Biol. Chem. (**1998**), 273(15), 8799-8805
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 15-5 (Immunochemistry)
AB The authors previously reported that interleukin-1 (IL-1) promoted the survival of murine **osteoclast**-like cells (OCLs) formed in vitro and activated a transcription factor, **NF-.kappa.B**, of OCLs. The present study examd. whether the activation of **NF-.kappa.B** is directly involved in the survival of OCLs promoted by IL-1. The expression of IL-1 type I receptor mRNA in OCLs was detected by the PCR amplification of reverse-transcribed mRNA. An electrophoretic mobility shift assay showed that IL-1 transiently activated **NF-.kappa.B** in the nuclei of the OCLs, and the maximal activation occurred at 30 min. The degrdn. of I.**kappa.B**.alpha. coincided with the

joint has been assocd. with rheumatoid arthritis (RA), its significance is poorly understood. Here, the authors examine the role of **NF-.kappa.B** in animal models of RA. The authors demonstrate that in vitro, **NF-.kappa.B** controlled expression of numerous inflammatory mols. in synoviocytes and protected cells against tumor necrosis factor .alpha. (TNF.alpha.) and Fas ligand (FasL) cytotoxicity. Similar to that obsd. in human RA, **NF-.kappa.B** was activated in the synovium of rats with streptococcal cell wall (SCW)-induced arthritis. In vivo suppression of **NF-.kappa.B** by either **proteasomal** inhibitors or intraarticular adenoviral gene transfer of super-repressor I.**kappa.B**.alpha. profoundly enhanced apoptosis in the synovium of rats with SCW- and pristane-induced arthritis. This indicated that the activation of **NF-.kappa.B** protected the cells in the synovium against apoptosis and thus provided the potential link between inflammation and hyperplasia. Intraarticular administration of **NF**-kB decoys prevented the recurrence of SCW arthritis in treated joints. Unexpectedly, the severity of arthritis also was inhibited significantly in the contralateral, untreated joints, indicating beneficial systemic effects of local suppression of **NF-.kappa.B**. These results establish a mechanism regulating apoptosis in the **arthritic joint** and indicate the feasibility of therapeutic approaches to RA based on the specific suppression of **NF-.kappa.B**.

ST transcription factor NFkappaB cytokine inflammation hyperplasia rheumatoid arthritis

IT Apoptosis
Rheumatoid arthritis
Synoviocyte
Transcriptional activation
(**NF-.kappa.B** activation in inflamed synovium activates inflammatory cytokines but inhibits TNF.alpha.- and FasL-mediated apoptosis thereby promoting hyperplasia in animal models of rheumatoid arthritis)

IT **NF-.kappa.B**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**NF-.kappa.B** activation in inflamed synovium activates inflammatory cytokines but inhibits TNF.alpha.- and FasL-mediated apoptosis thereby promoting hyperplasia in animal models of rheumatoid arthritis)

IT Fas ligand
Interleukin 1.beta.
Interleukin 6
Tumor necrosis factor .alpha.
VCAM-1 (cell adhesion molecule)
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(**NF-.kappa.B** activation in inflamed synovium activates inflammatory cytokines but inhibits TNF.alpha.- and FasL-mediated apoptosis thereby promoting hyperplasia in animal models of rheumatoid arthritis)

IT **Synovial membrane**
(**disease, synovitis; NF-.kappa.B** activation in inflamed synovium activates inflammatory cytokines but inhibits TNF.alpha.- and FasL-mediated apoptosis thereby promoting hyperplasia in animal models of rheumatoid arthritis)

IT **Synovial membrane**
(hyperplasia; **NF-.kappa.B** activation in inflamed synovium activates inflammatory cytokines but inhibits TNF.alpha.- and FasL-mediated apoptosis thereby promoting hyperplasia in animal models of rheumatoid arthritis)

IT Hyperplasia
(synovial; **NF-.kappa.B** activation in inflamed synovium activates inflammatory cytokines but inhibits TNF.alpha.- and FasL-mediated apoptosis thereby promoting hyperplasia

activation of **NF-.kappa.B** in the OCLs. The immunocytochem. study revealed that p65, a subunit of **NF-.kappa.B**, was translocated from the cytoplasm into almost all of the nuclei of the OCLs within 30 min after IL-1 stimulation. The purified OCLs spontaneously died via apoptosis, and IL-1 promoted the survival of OCLs by preventing their apoptosis. The pretreatment of purified OCLs with **proteasome** inhibitors suppressed the IL-1-induced activation of **NF-.kappa.B** and prevented the survival of OCLs supported by IL-1. When OCLs were pretreated with antisense oligodeoxynucleotides to p65 and p50 of **NF-.kappa.B**, the expression of resp. mRNAs by OCLs was suppressed, and the IL-1-induced survival of OCLs was concomitantly inhibited. Thus, IL-1 promotes the survival of **osteoclasts** through the activation of **NF-.kappa .B.**

ST NF kappaB survival **osteoclast** interleukin 1

IT Apoptosis
Osteoclast
(interleukin-1 promotes **osteoclasts** survival by preventing apoptosis via **NF-.kappa.B** activation)

IT Interleukin 1
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(interleukin-1 promotes **osteoclasts** survival by preventing apoptosis via **NF-.kappa.B** activation)

IT **NF-.kappa.B**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(interleukin-1 promotes **osteoclasts** survival by preventing apoptosis via **NF-.kappa.B** activation)

L193 ANSWER 3 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 1997:300447 BIOSIS
DN PREV199799599650
TI The **trental** influence on collagen proteolysis in experimental aseptic infarction of the **long bone**.
AU Magomedov, S.; Grigorovskii, V. V.
CS Ukr. Res. Inst. Traumatol. Orthop., Ukr. Minist. Health, Kiev Ukraine
SO Ukrainskii Biokhimicheskii Zhurnal, (1996) Vol. 68, No. 5, pp. 69-76. ISSN: 0201-8470.
DT Article
LA Russian
SL Ukrainian; English
AB Dynamics of biochemical parameters of the connective tissue and morphometric parameters of lesion were studied in rabbits with induced embolic aseptic infraction of the femur without and with the **trental** (**pentoxyphyllin**) treatment. The correlation was found between the pairs of indices: proteolytic activity and bone marrow necrosis volume: collagenase activity and bone cortex remodelling rate: concentration of protein bound with hydroxyprolin fraction and endosteal regenerate volume.
CC Biochemical Studies - General *10060
Cardiovascular System - General; Methods *14501
Bones, Joints, Fasciae, Connective and Adipose Tissue - General; Methods *18001
Pharmacology - General *22002
BC Leporidae *86040
IT Major Concepts
Biochemistry and Molecular Biophysics; Cardiovascular System (Transport and Circulation); Pharmacology; Skeletal System (Movement and Support)
IT Chemicals & Biochemicals
TRENTAL; PENTOXIFYLLINE; COLLAGENASE
IT Miscellaneous Descriptors
ASEPTIC INFARCTION; BONE CORTEX REMODELLING RATE; BONE DISEASE; BONE MARROW NECROSIS VOLUME; COLLAGEN PROTEOLYSIS; COLLAGENASE ACTIVITY; ENDOSTEAL REGENERATE VOLUME; EXPERIMENTAL; FEMUR; **LONG BONE; PENTOXIFYLLINE; PENTOXYPHYLLIN;**

PHARMACOLOGY; SKELETAL SYSTEM; **TRENTAL** INFLUENCE; VASCULAR DISEASE; VASODILATOR-DRUG
ORGN Super Taxa
Leporidae: Lagomorpha, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rabbit (Leporidae)
ORGN Organism Superterms
animals; chordates; lagomorphs; mammals; nonhuman mammals; nonhuman vertebrates; vertebrates
RN **6493-05-6 (TRENTAL)**
6493-05-6 (PENTOXIFYLLINE)
9001-12-1 (COLLAGENASE)

L193 ANSWER 4 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:561734 BIOSIS
DN PREV200100561734
TI Regulation of osteoblast differentiation by **proteasome** control of Smad1.
AU Chen, D. (1); Zhao, M. (1); Qiao, M. (1); **Garrett, R. (1)**; Mi, Z. (1); Crews, C.; **Mundy, G. (1)**
CS (1) Medicine, University of Texas Health Science Center at San Antonio, San Antonio, TX USA
SO Journal of Bone and Mineral Research, (September, 2001) Vol. 16, No. Suppl. 1, pp. S145. print.
Meeting Info.: Twenty-Third Annual Meeting of the American Society for Bone and Mineral Research Phoenix, Arizona, USA October 12-16, 2001
ISSN: 0884-0431.
DT Conference
LA English
SL English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
Cytology and Cytochemistry - Animal *02506
Bones, Joints, Fasciae, Connective and Adipose Tissue - Physiology and Biochemistry *18004
BC Animalia - Unspecified 33000
IT Major Concepts
Skeletal System (Movement and Support)
IT Chemicals & Biochemicals
Smad-1 protein: osteoblast differentiation regulator, **proteasome** control
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Animalia
ORGN Organism Name
C2-C12 cell line (Animalia): myoblast-osteoblast precursor cell line, osteoblast differentiation
ORGN Organism Superterms
Animals

L193 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:413041 BIOSIS
DN PREV200000413041
TI Specific inhibitors of the chymotryptic component of the **proteasome** are potent bone anabolic agents in vivo.
AU **Garrett, I. R. (1)**; Gutierrez, G. (1); Chen, D. (1); **Rossini, G. (1)**; Escobedo, A. (1); Esparza, J. (1); Horn, D. (1); Crews, C. M.; **Mundy, G. R. (1)**
CS (1) OsteoScreen, Inc., San Antonio, TX USA
SO Journal of Bone and Mineral Research, (September, 2000) Vol. 15, No. Suppl. 1, pp. S197. print.
Meeting Info.: Twenty-Second Annual Meeting of the American Society for Bone and Mineral Research Toronto, Ontario, Canada September 22-26, 2000 American Society for Bone and Mineral Research
. ISSN: 0884-0431.

DT Conference
LA English
SL English
CC Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General *10060
Bones, Joints, Fasciae, Connective and Adipose Tissue - Physiology and Biochemistry *18004
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Muridae 86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Skeletal System (Movement and Support)
IT Parts, Structures, & Systems of Organisms
bone: formation, skeletal system; osteoblast: proliferation, skeletal system
IT Chemicals & Biochemicals
potent bone anabolic agent: in-vivo; specific chymotryptic **proteasome** component inhibitor; statins
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
murine (Muridae)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L193 ANSWER 6 OF 8 MEDLINE
AN 1998312293 MEDLINE
DN **98312293** PubMed ID: **9648487**
TI Hyperparathyroidism and its management.
AU Sugimoto T
CS Department of Medicine, Kobe University School of Medicine.
SO NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, **(1998 Jun)** 56 (6) 1591-7. Ref: 36
Journal code: KIM; 0420546. ISSN: 0047-1852.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA Japanese
FS Priority Journals
EM 199809
ED Entered STN: 19980917
Last Updated on STN: 19980917
Entered Medline: 19980908
AB Hyperparathyroidism (HPT), resulting from the excess of endogenous parathyroid hormone is cited as one of diseases which cause secondary osteoporosis. HPT consists of primary (1 degree) and secondary (2 degrees) HPT, resulting mainly from chronic renal failure (CRF). HPT is easily distingishable from primary osteoporosis by biochemical measurements. Parathyroidectomy (**PTX**) is the only option available for the radical cure of 1 degree HPT and more than 10% increase in bone mass occurs after **PTX**. On the other hand, dietary phosphorus restriction, phosphorus binders, active vitamin D3 metabolites are useful for 2 degrees HPT due to CRF. When these treatments are not effective to inhibit PTH secretion adequately, oral active vitamin D3 pulse therapy, **PTX** and percutaneous ethanol injection therapy should be considered.
CT Check Tags: Human
*Hyperparathyroidism: CO, complications
*Hyperparathyroidism: TH, therapy
Hyperparathyroidism, Secondary: CO, complications
***Osteoporosis: ET, etiology**

L193 ANSWER 7 OF 8 MEDLINE
AN 96302997 MEDLINE
DN **96302997** PubMed ID: **8741178**
TI Suppressive effect of N-(benzyloxycarbonyl)-L-phenylalanyl-L-tyrosinal on bone resorption in vitro and in vivo.
AU Woo J T; Yamaguchi K; Hayama T; Kobori T; Sigeizumi S; Sugimoto K; Kondo K; Tsuji T; Ohba Y; Tagami K; Sumitani K
CS Sagami Chemical Research Center, Kanagawa, Japan.
SO EUROPEAN JOURNAL OF PHARMACOLOGY, **(1996 Apr 4)** 300 (1-2) 131-5.
Journal code: EN6; 1254354. ISSN: 0014-2999.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199610
ED Entered STN: 19961025
Last Updated on STN: 19961025
Entered Medline: 19961017
AB The suppressive effect of N-(benzyloxycarbonyl)-L-phenylalanyl-L-tyrosinal on bone resorption was examined in vitro and in vivo. This synthetic **peptidyl aldehyde** was found to be a potent and selective cathepsin L inhibitor in our screening for cysteine protease inhibitors. In the pit formation assay with unfractionated rat bone cells, 1.5 nM of this compound markedly inhibited parathyroid hormone-stimulated osteoclastic bone resorption. In addition, intraperitoneal administration of this **peptidyl aldehyde** (2.5-10 mg/kg) for 4 weeks suppressed bone weight loss dose dependently in the ovariectomized mouse, experimental model of osteoporosis. Hydroxyproline measurement of the decalcified femurs from these ovariectomized mice suggested that this compound acts as a bone resorption suppressor through the inhibition of collagen degradation.
CT Check Tags: Animal; Female; Human
***Bone Resorption: PP, physiopathology**
***Bone and Bones: DE, drug effects**
Bone and Bones: ME, metabolism
*Cathepsins: AI, antagonists & inhibitors
*Cysteine Proteinase Inhibitors: PD, pharmacology
*Dipeptides: PD, pharmacology
Leucine: AA, analogs & derivatives
Leucine: PD, pharmacology
Mice
Ovariectomy
Rats
Rats, Sprague-Dawley
RN 66701-25-5 (E 64); 7005-03-0 (Leucine)
CN 0 (Cysteine Proteinase Inhibitors); 0 (Dipeptides); 0 (N-(benzyloxycarbonyl)-phenylalanyl-tyrosinal); EC 3.4.- (Cathepsins); EC 3.4.22.15 (cathepsin L)

L193 ANSWER 8 OF 8 MEDLINE
AN 83293098 MEDLINE
DN **83293098** PubMed ID: **6310016**
TI Studies on osteoporoses. XI. Effects of a methylxanthine derivative. A preliminary report.
AU Robin J C; Ambrus J L
SO JOURNAL OF MEDICINE, **(1983)** 14 (2) 137-45.
Journal code: IYG; 7505566. ISSN: 0025-7850.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198310
ED Entered STN: 19900319
Last Updated on STN: 19900319
Entered Medline: 19831021

AB Heparin (500 U/kg s.c. B.I.D.) induced significant osteoporosis in C3H/St(Ha) female mice after 3 months of treatment. **Pentoxifylline** (12 mg/kg i.m. B.I.D.) prevented this experimental osteoporosis. Osteoporosis was measured by in vivo neutron activation analysis and results were confirmed by atomic absorption spectroscopy. **Pentoxifylline** (0.1-100 microgram/ml) increased calcium uptake and cAMP production in osteoblast-like bone cells isolated from fetal Sprague-Dawley rats. Theoretical implications for osteoblast control of bone resorption are discussed.

CT Check Tags: Animal; Female
Bone Resorption
Calcium: ME, metabolism
Cyclic AMP: ME, metabolism
Heparin
Mice
Mice, Inbred C3H
Neutron Activation Analysis
Osteoblasts: DE, drug effects
Osteoblasts: ME, metabolism
Osteoporosis: CI, chemically induced
***Osteoporosis: PC, prevention & control**
***Pentoxifylline: TU, therapeutic use**
Rats
Rats, Inbred Strains
Spectrophotometry, Atomic Absorption
Stimulation, Chemical
*Theobromine: AA, analogs & derivatives

RN 60-92-4 (Cyclic AMP); **6493-05-6 (Pentoxifylline)**; 7440-70-2 (Calcium); 83-67-0 (Theobromine); 9005-49-6 (Heparin)

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L215 ANSWER 1 OF 2 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2000-686989 [67] WPIX
DNC C2000-208928
TI Identifying a compound effective in treating multiple myeloma and myeloma bone disease, involves subjecting the compound to an assay determining its ability to inhibit NF-kB or proteasomal activity.
DC B04
IN **MUNDY, G R**
PA (OSTE-N) **OSTEOSCREEN INC**
CYC 22
PI WO 2000061167 A2 20001019 (200067)* EN 22p A61K038-04
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP

AU 2000042040 A 20001114 (200108) A61K038-04
EP 1169049 A2 20020109 (200205) EN A61K038-04
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 2000061167 A2 WO 2000-US9121 20000407; AU 2000042040 A AU 2000-42040 20000407; EP 1169049 A2 EP 2000-921764 20000407, WO 2000-US9121 20000407
FDT AU 2000042040 A Based on WO 200061167; EP 1169049 A2 Based on WO 200061167
PRAI US 1999-289229 19990409
IC ICM A61K038-04
ICS A61K031-166; A61K031-40; A61P019-08
AB WO 200061167 A UPAB: 20001223
NOVELTY - Identifying a compound (I) effective in treating myeloma bone disease involves subjecting the compound to an assay to determine its ability to inhibit transcription factor NF-kB activity or production, or to an assay to determine its ability to inhibit proteasomal enzyme activity or production.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a pharmaceutical composition for treating myeloma bone disease comprising (I); and
(2) a method of treating myeloma bone disease by the administration of (I).
ACTIVITY - Osteopathic; cytostatic.
Nine C57BL/KaLwRij mice were inoculated with 0.5 asterisk 106 5TGM-1 cultured myeloma cells and tumor volume was assessed by the formula Tumor volume (cm3) = 4/3((length + width)-1)/2. The mice with tumors were randomized into two groups and treatment was commenced on day 35. One group has **PSI** injected directly into the tumors and the other group has only vehicle injected into the tumors. The tumors in the latter group (untreated mice) continued to grow, resulting in the mice dying between 42 and 55 days after myeloma cell inoculation. The size of the tumors in the treated mice decreased markedly and the mice remained healthy up to 3 months after tumor inoculation, even though treatment was discontinued. The result showed that the treated mice were alive and well with no signs of tumor 4 months after treatment.
MECHANISM OF ACTION - Inhibitor of NF-kB activity; inhibitor of proteasomal activity.
(I) reduces myeloma tumor volume, delays onset of limb paralysis, decreases the viability of myeloma cells and reduces the volume of tumor marker, IbG2b. (claimed).
USE - (I) is useful for treating multiple myeloma such as osteopenia, osteolytic lesions, osteopetrosis, bone fracture and osteolytic bone disease, and myeloma bone disease (claimed).
Dwg.0/6
FS CPI
FA AB; DCN
MC CPI: B04-C01A; B10-A06; B10-A12A; B14-H01; B14-H01A; B14-L06

L215 ANSWER 2 OF 2 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2000-171065 [15] WPIX
DNC C2000-053186
TI Compound that inhibits the activity of NF-kappa B useful for enhancing bone formation.
DC B04 B05
IN **GARRETT, I R; MUNDY, G R; ROSSINI, G**
PA (OSTE-N) **OSTEOSCREEN**; (OSTE-N) **OSTEOSCREEN INC**
CYC 73
PI WO 2000002548 A2 20000120 (200015)* EN 37p A61K031-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AL AM AU BA BB BG BR CA CN CU CZ EE GE HU IL IN IS JP KP KR LC LK LR LT LV MD MG MK MN MX NO NZ PL RO SD SG SI SK TR TT US UZ VN
AU 9963109 A 20000201 (200028) A61K031-00
EP 1096924 A1 20010509 (200128) EN A61K031-00
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 2000002548 A2 WO 1999-US15533 19990709; AU 9963109 A AU 1999-63109 19990709; EP 1096924 A1 EP 1999-933827 19990709, WO 1999-US15533 19990709

FDT AU 9963109 A Based on WO 200002548; EP 1096924 A1 Based on WO 200002548
PRAI US 1998-113947 19980710
IC ICM A61K031-00
AB WO 200002548 A UPAB: 20000323
NOVELTY - Enhancing bone formation, treating pathological dental conditions, treating degenerative joint conditions by administration of NF-kappa B inhibitor.

DETAILED DESCRIPTION - Enhancing bone formation or treating pathological dental conditions or treating degenerative joint conditions in a vertebrate animal comprises administration of a compound that inhibits the activity of NF-kB or that inhibits **proteasomal** activity or that inhibits production of **proteasome** proteins.

INDEPENDENT CLAIMS are included for the following:

(1) treatment of a condition benefited by stimulating hair growth comprising administration of a compound that inhibits the activity of NF-kB or that inhibits **proteasomal** activity or that inhibits production of these proteins, and

(2) identifying a compound which enhances bone growth or stimulates hair growth comprising subjecting a candidate compound to an assay to assess its ability to inhibit:

(a) NF-kB activity, or

(b) the production of NF-kB, or

(c) **proteasomal** activity, or

(d) the production of enzymes with **proteasomal** activity,

where for all the inhibitory compound is identified as a compound that enhances bone growth.

ACTIVITY - Osteopathic; Endocrine-Gen.; Screening; Vulnerary. **PSI** (N-carbobenzoyl-Ile-Glu-(OtBu)-Ala-Leu-CHO) was assayed in vitro for calvarial bone growth. Administered at 0.1, 1 and 5 mg/kg/day, the % increase in bone area compared to control was 21.7, 35.4 and 32.1%, respectively. The 1 and 5 mg/kg/day doses produced an increase in new bone width of 19.9%.

MECHANISM OF ACTION - Antimetastatic; Nuclear-Factor-Inhibitor-Kappa-B.

USE - The method can be used for enhancing bone formation, treating pathological dental conditions, degenerative bone conditions, osteoporosis, bone fracture or deficiency, primary or secondary hyperparathyroidism, periodontal disease or defect, metastatic bone disease, osteolytic bone disease, post-plastic surgery, post-prosthetic joint surgery, and post-dental implantation, and for stimulating hair growth (claimed). The compounds may also be useful in wound healing or tissue repair.

ADVANTAGE - None given.

Dwg.0/1
FS CPI
FA AB; DCN
MC CPI: B04-C01; B06-D13; B06-F05; B07-A02B; B07-D03; B10-A06; B10-A10; B10-D02; B11-C08; B12-K04A; B14-D03; **B14-N01**; **B14-N06**; B14-N11; B14-N17B; **B14-R02**
TECH UPTX: 20000323
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The compound does not inhibit the isoprenoid pathway. The compound is **lactacystin**, a peptidyl aldehyde or PTX. The method further comprises administration of one or more agents that promote bone growth or that inhibit bone resorption such as bone morphogenetic factors, anti-resorptive agents, osteogenic factors, cartilage-derived morphogenetic proteins, growth hormones, estrogens, bis phosphonates, statins or differentiating factors.